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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/779,460	01/07/1997	OSCAR JOHANNES MARIA GODDIJN	U-011098-6	5897

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EXAMINER

FOX, DAVID T

ART UNIT	PAPER NUMBER
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1638

DATE MAILED: 07/12/2002

32

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/779,460

Applicant(s)

Goddijn et al

Examiner

FOX

Group Art Unit

1638

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 4/6/01 + 6/13/01
- ☐ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 25, 35-65 is/are pending in the application.
- Of the above claim(s) 37-38, 43, 51-55, 57, 58, 63, 64 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 25, 35, 36, 39-41, 43-50, 56, 59-62, 65 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
 - ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
 - ☐ received in Application No. (Series Code/Serial Number) _____
 - ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other _____

Office Action Summary

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The request filed on 6 April 2001 and perfected on 13 June 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 08/779,460 is acceptable and a CPA has been established. An action on the CPA follows.

Applicants' petition under 37 CFR 1.103(a) of 13 June 2001 for a sixth month suspension has been granted, as indicated in the Decision mailed 21 June 2001. Since more than six months have transpired, and Applicants have not requested further suspension, prosecution is resumed. See MPEP 709.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25, 35-36, 39-41, 43-50, 56, 59-62 and 65, drawn to Species A, namely a method for trehalase inhibition in plants comprising a trehalose synthesis gene, wherein said trehalase inhibition is accomplished via chemical treatment with a trehalase inhibitor, remain examined, as stated in the Office action of 6 November 2000. Claim 25 is generic to Species A and Species B, namely an antisense RNA-mediated method for inhibiting trehalase. Non-elected claims 37-38, 42, 51-55, 57-58 and 63-64 remain withdrawn from consideration, as stated in the Office action of 6 November 2000.

Claims 48, 61 and 62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 48 is indefinite in its recitation of "the steps of producing trehalose in *plant cells*" (emphasis added) which lacks antecedent basis in claim 35.

Claims 61-62 are indefinite in their recitation of "process according to claim 44" which is confusing, since claim 44 is drawn to a product rather than a process. Amendment of claim 61 to replace "44" with --43-- or with --59-- would obviate this rejection.

Claims 25, 35-36, 39-41, 43-50, 56, 59-62 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a method for producing trehalose in plants transformed with a bacterial or fungal gene encoding trehalose phosphate synthase wherein the plants are treated with a chemical trehalase inhibitor comprising validamycin, does not reasonably provide enablement for claims broadly drawn to plants which naturally produce trehalose or chemical treatment thereof, the use of any other transgene encoding any other gene product, or the use of non-validamycin chemical trehalase inhibitors. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn to the inhibition of trehalase in plants which produce trehalose via the introduction of a gene from any source encoding any bipartite trehalose synthesizing enzyme (claim 25), or in a multitude of plants which either naturally produce trehalose or which have been "genetically altered" in some way to produce trehalose (claim 35 and dependents), wherein such genetic alteration may include mutation or upregulation of

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endogenous trehalose biosynthesis genes, wherein such trehalase inhibition is obtained via the application of a multitude of chemical trehalase inhibitors.

In contrast, the specification only demonstrates the inhibition of trehalase in plants which have been transformed with an *E. coli* trehalose phosphate synthase (TPS) gene, wherein such plants have been treated with validamycin. In addition, the specification discloses that other workers have isolated a TPS gene from yeast, and Applicants have provided publications demonstrating plant transformation therewith. However, no guidance has been provided regarding the identification of any other enzyme involved in trehalose synthesis or the isolation of the corresponding gene encoding it, other than TPS. Furthermore, no guidance has been provided regarding the identification or isolation of TPS or its encoded gene in any other organism such as plants or animals, or regarding the upregulation or mutagenesis of any endogenous trehalose biosynthesis gene in plants. In addition, no guidance has been provided regarding chemical treatment of the single plant known to produce trehalose naturally, namely the resurrection plant. Finally, no guidance has been provided regarding the use of a multitude of non-exemplified chemical trehalase inhibitors.

Trehalose production is extremely rare in plants, as taught by Kendall et al (see, e.g., page 2525, column 1, top paragraph). One of the few plants in which it occurs is the resurrection plant, *Selaginella lepidophylla* (page 2525, column 2, bottom paragraph). Thus, it is unpredictable and unlikely that a multitude of plants would naturally produce trehalose, as broadly

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claimed in claim 35. In addition, the waxy coating of the resurrection plant would not lend itself to chemical application of a trehalase inhibitor.

The production of trehalose in plants not transformed with a bacterial or fungal TPS gene is unpredictable and unlikely. Goddijn et al (1997) teach that trehalose synthesis requires TPS (see, e.g., page 181, column 2, bottom paragraph). Furthermore, it is unpredictable that a multitude of plants or animals would possess the necessary enzymes for trehalose synthesis including TPS, or the genes encoding them, so that the isolation of genes encoding either the exemplified trehalose synthesis enzyme from a multitude of non-exemplified sources, or the isolation of genes encoding a multitude of non-exemplified trehalose synthesis enzymes, is unpredictable and unlikely, wherein said isolation would be required in order to practice the invention as broadly claimed.

The inhibition of trehalase in plants which produce trehalose is unpredictable. Veluthambi et al teach that trehalose is toxic to higher plants which do not naturally produce it, wherein such toxicity is exacerbated by trehalase inhibition, wherein trehalase would otherwise degrade the trehalose (see, e.g., page 1369, Abstract).

In addition, plant transformation with genes encoding trehalose synthesis enzymes is unpredictable. Goddijn et al (1997) teach that such transformation of tobacco resulted in stunting of plants and reduction in leaf size, as well as leaf bleaching (see, e.g., page 185, column 1, top paragraph; paragraph bridging pages 185 and 186), while potato transformation resulted in

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reduced root growth (see, e.g., paragraph bridging pages 185 and 186). Thus, the inhibition of trehalase would appear to exacerbate these toxic effects.

Finally, different trehalase inhibitors have different modes of action, and so the behavior of a multitude of non-exemplified chemical trehalase inhibitors in the instantly claimed method would be unpredictable, as set forth in the Office action of 30 March 2000, pages 8-10.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify a multitude of non-exemplified plants which naturally produce trehalose, to develop and evaluate methods for the “genetic alteration” of plants to produce trehalose via a multitude of non-exemplified means such as mutation or upregulation of endogenous trehalose synthesis genes, to identify and isolate a multitude of non-exemplified trehalose biosynthesis enzymes and the genes encoding them, to isolate TPS genes from a multitude of non-exemplified sources, to evaluate the ability of a multitude of non-exemplified trehalose biosynthesis genes to produce trehalose in transformed plants, or to evaluate a multitude of non-exemplified trehalase inhibitors for their ability to increase trehalose production and increase stress resistance without killing plants.

Claims 25, 35-36, 39-41, 43-50, 56, 59-62 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

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The claims are broadly drawn to plant transformation with a multitude of non-exemplified genes from a multitude of non-exemplified sources and of a multitude of non-exemplified sequences, which encode a multitude of non-exemplified trehalose biosynthesis enzymes. In contrast, the specification only provides guidance for plant transformation with the yeast or *E. coli* trehalose phosphate synthase genes. No guidance is provided for any TPS gene or its sequence from any other source, and no guidance is provided for the characterization of any other trehalose biosynthesis enzyme or its corresponding gene from any source. No conserved or diagnostic structural features responsible for trehalose biosynthesis were identified in any protein or its encoded gene.

Given the claim breadth and lack of guidance as discussed above, the specification does not adequately characterize the broadly claimed genus. Accordingly, one skilled in the art would not have recognized Applicants to have been in possession of the broadly claimed invention.

See Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

See *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

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The claims remain free of the prior art, as stated in the Office action of 6 November 2000.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is (703) 308-0280. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached on (703) 306-3218. The fax phone number for this Group is (703) 872-9306. The after final fax phone number is (703) 872-9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

July 8, 2002

DAVID T. FOX
PRIMARY EXAMINER
GROUP 180-1638

A handwritten signature in black ink, appearing to read "David T. Fox", with a stylized flourish at the end.